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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
MORRIS, PATRICIA L	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/593,801	ZAHN ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-78 and 80-85* is/are pending in the application.

4a) Of the above claim(s) *8-11,13,20,32-36,42-72,74 and 80-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,14,15,17,19,22-26,37-39,41,73 and 78* is/are rejected.

7)☒ Claim(s) *2,5,6,12,16-18,21,27-31 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 12, 14-19, 21-31, 37-41, 73 and 75-78 are under consideration in this application.

Claims 8-11, 13, 20, 32-36, 42-72, 74 and 80-85 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

Election/Restrictions

Applicant's election with traverse of Group I and compound no. 5 in the reply filed on September 24, 2010 is acknowledged. The traversal is on the ground that the compounds contain additional heteocycles is not found persuasive for the reasons clearly set forth in the previous Office action. Applicants' claims embrace the entire field of heterocyclic chemistry and that is why the additional heterocycles have been restricted out. In these claims, the numerous variables and their voluminous complex meaning and their seemingly endless permutations and combinations, make it virtually impossible to determine the full scope and complete meaning of the claimed subject matter. The variable cores created by A, X, D, etc., do not even belong to a recognized class of compounds. The international search report recites that claims 1-38 related to an extremely large number of possible compounds that it was impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought. Only a few compounds are exemplified in the specification. Further, the reports states that a meaningful search over the whole breadth of the claims is impossible. Moreover, applicants have failed to advance any cogent reasons as to why the inventions do not lack unity of invention. The request for rejoining claim 85 with the elected compound cannot be made because it is evidenced that it is well recognized in the art that alpha5beta1 integrin is a class of

enzymes involved in many regulatory mechanisms with other enzymes and physiological systems. There is no evidence of record that the instant compounds are able to treat and prevent all disorders associated with an alpha5beta1 integrin. A claim to all alpha5beta 1 integrin mediated disorders is considered a reach through to the continuous development of the field and do not meet the requirements of 35 U.S.C. 112.

It is too burdensome for the examiner to search all of the previously noted searches in their respective, completely divergent, areas for the non-elected subject matter, as well, in the limited time provided to search one invention.

The restriction requirement is deemed sound and proper and will be maintained.

It is unclear what variables are drawn to the elected compounds in claim 1 and applicants have failed to specify what claims correspond to the elected compounds in the instant response. However, this application has been examined to the extent readable on the elected compounds wherein D is (optionally substituted) pyrrolidne wherein X is attached to the N of the pyrrolidine ring, X is (CO)O, A is (optionally substituted) benzyl or phenyl, Z is alkylene, G is (optionally substituted) pyridin-2-yl, Y is O-CH_n-NH-$(CH_2)_n$, B represents non-heterocyclic groups and n as set forth in claim 1, exclusively. All additional heterocyclic compounds pertain to nonelected subject matter.

Claim Rejections - 35 USC э 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 75 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is a lack of description as to how the forms such as the hydrates or solvates are produced and what the hydrates or solvates are produced in the specification. Vippagunta et al. states on page 11 states the main challenge in managing the phenomenon of multiple solid forms of a drug is the inability to predict the number of forms that can be expected in a given case. Further, Vippagunta et al. recites on page 18 that predicting the formation of solvates of a compound and the number of molecules of solvent or water incorporated into the crystal lattice of a compound is complex and difficult. Guillory in Brittain ed, pages 182-226 teach that solvates are formed by recrystallization of drug substances. However, not all compounds will form solvates or hydrates.

Claim 75 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparing the compounds and their salts does not reasonably provide enablement for any and all unknown solvates or hydrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The expression solvate is employed in claim 75 with no indication given as to what the solvates really are.

One should be able, from a reading of the claims, determine what that claim does or does not encompass.

Why? Because that claim precludes others from making, using, or selling that compound for 20 years. Therefore, one must know what compound is being claimed.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of compounds, their salts and solvates/hydrates.

State of the Prior Art

Hydrates and solvates can have very different properties. Solvates, etc., tend to convert from less stable to more stable forms. No method exists to predict what hydrate, solvate, etc., will work with any significant certainty. Predicting the formation of solvates and hydrates of a compound and the number of molecules of solvent or water incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible

formation of solvates of hydrates and hence generalizations cannot be made for a series of compounds. Note section 3.4 of Vippaguanta et al. Solvates, etc., can convert from one form to another during the manufacturing process of a pharmaceutical drug and will change the pharmacological affects of the drug. This is why it is important to monitor the compounds during manufacture of the drug to see if it persists during manufacture.

The amount of direction or guidance and the presence or absence of working examples

The specification fails to describe any hydrates or solvates. Solvates, etc., often change into other forms during drug manufacture. Based on the unpredictability in the art, applicants are not entitled to any and all unknown hydrates or solvates.

The written description is considered inadequate here in the specification. Conception of the intended group should not be the role of the reader. Applicants should, in return for a 20 year monopoly, be disclosing to the public that which they know as an actual demonstrated fact. The disclosure should not be merely an invitation to experiment. This is a 35 USC 112, first paragraph. If you (the public) find that it works, I claim it, is not a proper basis of patentability. In re Kirk, 153 USPQ 48, at page 53.

The breadth of the claims

The breadth of the claims are drawn to all potential hydrates and solvates in addition to the instant compounds.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the compounds and their unknown other forms being claimed.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant other forms are enabled by the instant application.

Genentech Inc v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and [p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claims 1, 7, 14, 15, 22-26, 37 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The expressions substituted and derivatives are employed with considerable abandon in claims 1, 7, 14, 15, 22-26, 37 and 39 with no indication given as to what the groups really are.

One should be able, from a reading of the claims, determine what that claim does or does not encompass.

Why? Because that claim precludes others from making, using, or selling that compound for 20 years. Therefore, one must know what compound is being claimed.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of compounds and their salts.

State of the Prior Art

Substituents and derivatives can have very different properties. Substituents and derivatives tend to convert from less stable to more stable forms. No method exists to predict what substituent will work with any significant certainty. Substituents and derivatives can convert from one form to another during the manufacturing process of a pharmaceutical drug and will change the pharmacological affects of the drug. This is why it is important to monitor the compounds during manufacture of the drug to see if it persists during manufacture.

The amount of direction or guidance and the presence or absence of working examples

The specification fails to describe any substituent. Substituents and derivatives often change into other forms during drug manufacture. Based on the unpredictability in the art, applicants are not entitled to any and all unknown substituents and derivatives.

The breadth of the claims

The breadth of the claims is drawn to the preparation of the compounds and their salts.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the process of preparing all unknown substituents.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Genentech Inc v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and [p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 7, 14, 15, 17, 19, 22-26, 37-39, 41, 73 and 75-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expressions substituted and derivatives in claims 1, 7, 14, 15, 22, 24, 37 and 39 are indefinite to their meaning.

The expression solvate in claim 75 is indefinite.

The term "comprising" in claims 1, 3, 4, 7, 14, 15, 17, 19, 22-38 and 41 is open-ended because it allows for the inclusion of other active ingredients.

Regarding claims 1, 22, 37 and 39, the phrases "preferably" and "more preferably" render the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claims 77 and 78 provides for the use of treating a disease, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 77 and 78 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 77 and 78 are recited as composition claims. However, they are drafted in terms of use. Composition claims are drawn to a producs and an inert carrrier only. Moreover, claims 73, 77 and 78 appear to be substantial duplicates.

Claim 76 is indefinite since it is unclear how a composition can contain a single dose and multiple doses at the same time. What are the ingredients of the composition?

The claims measure the invention. United Carbon Co. v. Binney & Smith., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, "Claims measure invention and resolution of invention must be based on what is claimed".

The C.C.P.A. in 1978 held "that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim": In re Priest, 199 USPQ 11, at 15.

Allowable Subject Matter

Claim 1 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and if rewritten directed solely to the subject matter indicated as being examinable, supra.

Claims 3, 4, 7, 14, 15, 17, 19, 22-26, 37-39, 41, 73 and 75-78 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims and if rewritten directed solely to the elected compounds.

Claims 2, 5, 6, 12, 16-18, 21, 27-31 and 40 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and if rewritten directly solely to the elected compounds.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Patricia L. Morris/
Primary Examiner, Art Unit 1625

plm
November 29, 2010